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FIG. 1A

CCGGGTCGACCCACGCGTCCGAAGGCCCCCTCTCACTCCGCTCCACTCCTCGGGCTGG
CTCTCCTGAGGATGCACCAGCGTCACCCCCGGGCAAGATGCCCTCCCCTCTGTGTGGC
CGGAATCCTTGCCTGTGGCTTTCTCCTGGGCTGCTGGGGACCCTCCCATTTCCAGCAGA
GTTGTCTTCAGGCTTTGGAGCCACAGGCCGTGTCTTCTTACTTGAGCCCTGGTGCTCCC
TTAAAAGGCCGCCCTCCTTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCGGG
CTGCAGGCGGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCCGATGTCTTCCA
GGCTCACCAGGAGGACACAGAGCGCTATGTGCTCACCAACCTCAACATCGGGGCAGAA
CTGCTTCGGGACCCGTCCCTGGGGGCTCAGTTTCGGGTGCACCTGGTGAAGATGGTCA
TTCTGACAGAGCCTGAGGGTGCTCCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
AGCGTCTGTGGGTGGAGCCAGACCATCAACCCTGAGGACGACACGGATCCTGGCCATG
CTGACCTGGTCCTCTATATCACTAGGTTTGACCTGGAGTTGCCTGATGGTAACCGGCAG
GTGCGGGGCGTCACCCAGCTGGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATTA
CCGAGGACACTGGCTTCGACCTGGGAGTCACCATTGCCCATGAGATTGGGCACAGCTT
CGGCCTGGAGCACGACGGCGCGCCCGGCAGCGGCTGCGGCCCCAGCGGACACGTGA
TGGCTTCGGACGGCGCCGCGCCCCGCGCCGGCCTCGCCTGGTCCCCCTGCAGCCGCC
GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGGCGCGCTGCGTGTGGGACCCGCCGC
GGCCTCAACCCGGGTCCGCGGGGCACCCGCCGGATGCGCAGCCTGGCCTCTACTACA
GCGCCAACGAGCAGTGCCGCGTGGCCTTCGGCCCCAAGGCTGTCGCCTGCACCTTCGC
CAGGGAGCACCTGGATATGTGCCAGGCCCTCTCCTGCCACACAGACCCGCTGGACCAA
AGCAGCTGCAGCCGCCTCCTCGTTCCTCTCCTGGATGGGACAGAATGTGGCGTGGAGA
AGTGGTGCTCCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCCATAGCAGCAGT
GCATGGGCGCTGGTCTAGCTGGGGTCCCCGAAGTCCTTGCTCCCGCTCCTGCGGAGGA
GGTGTGGTCACCAGGAGGCGGCAGTGCAACAACCCCAGACCTGCCTTTGGGGGGCGT
GCATGTGTTGGTGCTGACCTCCAGGCCGAGATGTGCAACACTCAGGCCTGCGAGAAGA
CCCAGCTGGAGTTCATGTCGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC
CTCCCCTGGCGGCGCCTCCTTCTACCACTGGGGTGCTGCTGTACCACACAGCCAAGGG
GATGCTCTGTGCAGACACATGTGCCGGGCCATTGGCGAGAGCTTCATCATGAAGCGTG
GAGACAGCTTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCCGGGAGGACGGGA
CCCTGAGCCTGTGTGTGTCGGGCAGCTGCAGGACATTTGGCTGTGATGGTAGGATGGA
CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGTGGTGGGGACAACAGCACGTGCAGC
CCACGGAAGGGCTCTTTCACAGCTGGCAGAGCGAGAGAATATGTCACGTTTCTGACAGT
TACCCCCAACCTGACCAGTGTCTACATTGCCAACCACAGGCCTCTCTTCACACACTTGG
CGGTGAGGATCGGAGGGCGCTATGTCGTGGCTGGGAAGATGAGCATCTCCCCTAACAC
CACCTACCCCTCCCTCCTGGAGGATGGTCGTGTCGAGTACAGAGTGGCCCTCACCGAG

OIPE JC10 30/31 JUN 18 2003 PATENT & T. ADMINISTRATION

FIG. 1B

GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAAACTACAGCTGCCTG
GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTGCGTGCTCGAACCCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCCTGCGGGAGCGGCCAGTGCGC
TGCGTGGAGGCCCAGGGCAGCCTCCTGAAGACATTGCCCCCAGCCCGGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC
AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGACTGAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCTGAGCCCTGTGTCGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG
TCGTGCTCCGTCTCCTGCGGGCGAGGTCTGATGGAGCTGCGTTTCCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTCGTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGGCT
GCCTCGCCCGGAACCCCAGGAGGCCTGCAGCCTGGAGCCCTGCCCACCTAGGTGGAA
AGTCATGTCCCTTGGCCCATGTTCGGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCCTGTGGGGATGGCATCCAGCG
CCGGCGTGACACCTGCCTCGGACCCCAGGCCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGACTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGCCCCTCGGGGAGGT
GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAGGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA
ATGCAGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGGCAGCAGGTGCTCTACTG

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FIG. 1C

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

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FIG. 2

PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLLGCWGPSHFQQSCL
QALEPQAVSSYLSPGAPLKGRPPSPGFQRQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINP
EDDTDPGHADLVLYITRFDLELPDGNRQVRGVTQLGGACSPTWSCLITEDTGFDLGVTIAHEI
GHSFGLEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRQLLSLLSAGRARCVWDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLLVPLLDGTECGVEKWCSKGRCRSLVELTPIAAVHGRWSSWGPRSPCSRSCGGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTRCMPSGPREDGTLSLCVS
GSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRAREYVTFLTVTPNLTSV
YIANHRPLFTHLAVRIGGRYVVAGKMSISPNTTYPSLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEEYGNLTRPDITFTYFQPKPRQAWVWAAVRGPCSVSCGAGLRWVN
YSCLDQARKELVETVQCQGSQQPPAWPEACVLEPCPPYWAVGDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQPAVALETCNPQPCPARWEVSEPSSCTSAGGAGLAL
ENETCVPGADGLEAPVTEGPGSVDEKLPAPEPCVGMSCPPGWGHLDATSAGEKAPSPWG
SIRTGAQAAHVWTPAAGSCSVSCGRGLMELRFLCMDSALRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVVRRILYCARAHGEDDGEEILLDTQCQGLPRPEPQE
ACSLEPCPPRWKVMSLGPCSASCGLGTARRSVACVQLDQGQDVEVDEAACAALVRPEASV
PCLIADCTYRWHVGTWMECSVSCGDGIQRRRDTCLGPQAQAPVPADFCQHLPKPVTVRGC
WAGPCVGQGTPSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCAVAIGR
PLGEVVTLRVLESSLNCSAGDMLLLWGRLTWRKMCRKLLDMTFSSKTNTLVVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAIHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

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FIG. 3A

Domain structure of ADAMTS-M and translated nucleic acid sequence. FIG. 3A Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). FIGS. 3B-3G ADAMTS-M nucleotide sequence with translated amino acid sequence above.

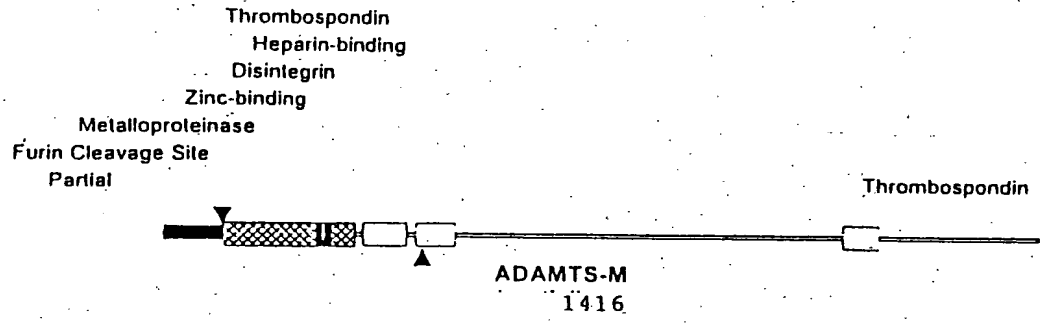

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FIG. 3B

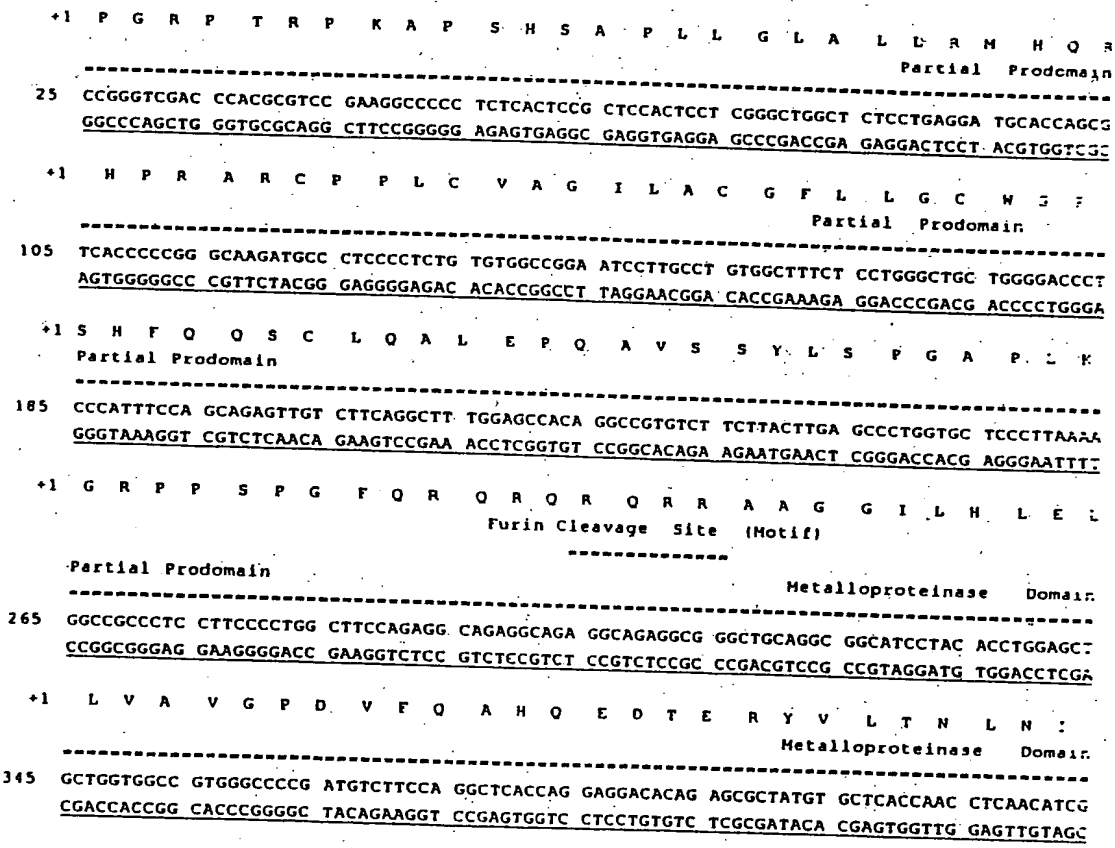

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FIG. 3C

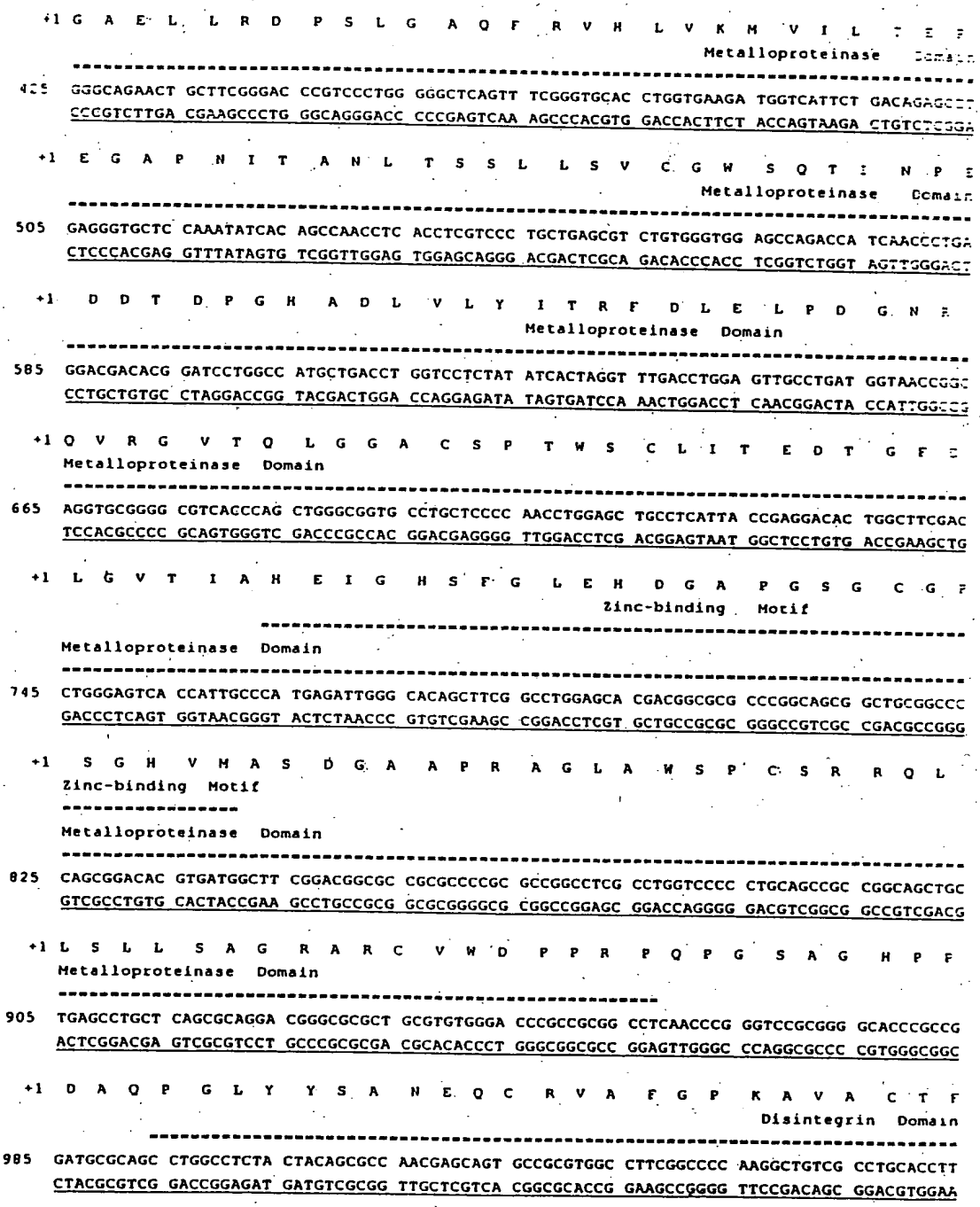

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FIG. 3D

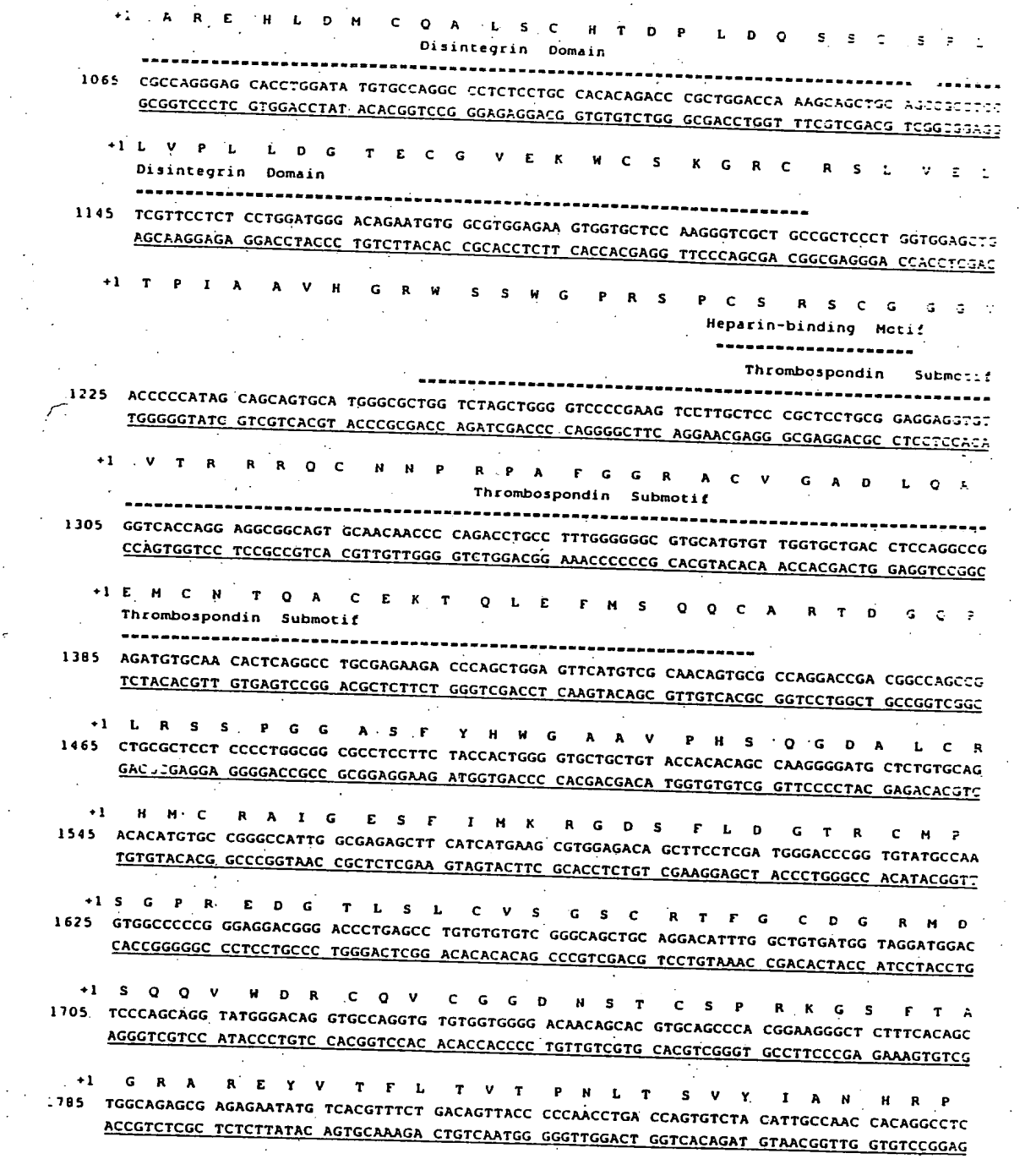

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FIG. 3E

```
     +1 L  F  T  H  L  A  V  R  I  G  G  R  Y  V  V  A  G  K  M  S  I  S  P  N  T  T  I
1965 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCCTAA CACTACCTAC
     AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGATG

     +1 P  S  L  L  E  D  G  R  V  E  Y  R  V  A  L  T  E  D  R  L  P  R  L  E  E  I  F
1945 CCCTCCCTCC TGGAGGATGG TCGTGTCGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCGCCTGG AGGAGATCCG
     GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTCTAGGC

     +1  I  W  G  P  L  Q  E  D  A  D  I  Q  V  Y  R  R  Y  G  E  E  Y  G  N  L  T  F
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCTTCC
     GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGCTCCT CATACCGTTG GAGTGGGCGG

     +1 P  D  I  T  F  T  Y  F  Q  P  K  P  R  Q  A  W  V  W  A  A  V  R  G  F  C  S  V
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCCTGGGTG TGGGCCGCTG TGCGTGGGCC CTGCTCGGTG
     GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCCGGCGAC ACGCACCCGG GACGAGCCAC

     +1 S  C  G  A  G  L  R  W  V  N  Y  S  C  L  D  Q  A  R  K  E  L  V  E  T  V  Q  I
2185 AGCTGTGGGG CAGGGCTGCG CTGGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTC
     TCGACACCCC GTCCCGACGC GACCCATTTG ATGTCGACGG ACCTGGTCCG GTCCTTCCTC AACCACCTCT GACAGGTCAG

     +1  Q  G  S  Q  Q  P  P  A  W  P  E  A  C  V  L  E  P  C  P  P  Y  W  A  V  G  E
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGGCG GTGGGAGACT
     GGTTCCCTCG GTCGTCGGTG GTCGCACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCTCTGA

     +1 F  G  P  C  S  A  S  C  G  G  L  R  E  R  P  V  R  C  V  E  A  Q  G  S  L  L
2345 TCGGCCCATG CAGCGCCTCC TGTGGGGGTG GCCTGCGGGA GCGGCCAGTG CGCTGCGTGG AGGCCCAGGG CAGCCTCCTG
     AGCCGGGTAC GTCGCGGAGG ACACCCCCAC CGGACGCCCT CGCCGGTCAC GCGACGCACC TCCGGGTCCC GTCGGAGGAC

     +1 K  T  L  P  P  A  R  C  R  A  G  A  Q  Q  P  A  V  A  L  E  T  C  N  P  Q  P  C
2425 AAGACATTGC CCCCAGCCCG GTGCAGAGCA GGGGCCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCCAGCCCTG
     TTCTGTAACG GGGGTCGGGC CACGTCTCGT CCCCGGGTCG TCGGTCGACA CCGCGACCTT TGGACGTTGG GGGTCGGGAC

     +1  P  A  R  W  E  V  S  E  P  S  S  C  T  S  A  G  G  A  G  L  A  L  E  N  E  T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCCAG CTCATGCACA TCAGCTGGTG GAGCAGGCCT GGCCTTGGAG AACGAGACCT
     GGGACGGTCC ACCCTCCACA GTCTCGGGTC GAGTACGTGT AGTCGACCAC CTCGTCCGGA CCGGAACCTC TTGCTCTGGA

     +1 C  V  P  G  A  D  G  L  E  A  P  V  T  E  G  P  G  S  V  D  E  K  L  P  A  P  E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGACTGA GGGGCCTGGC TCCGTAGATG AGAAGCTGCC TGCCCCTGAG
     CACACGGTCC CCGTCTACCG GACCTCCGAG GTCACTGACT CCCCGGACCG AGGCATCTAC TCTTCGACGG ACGGGGACTC

     +1 P  C  V  G  M  S  C  P  P  G  W  G  H  L  D  A  T  S  A  G  E  K  A  P  S  P  W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CCTCCCCATG
     GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCCGGTAG ACCTACGGTG GAGACGTCCC CTCTTCCGAG GGAGGGGTAC

     +1  G  S  I  R  T  G  A  Q  A  A  H  V  W  T  P  A  A  G  S  C  S  V  S  C  G  R
2745 GGGCAGCATC AGGACGGGGG CTCAAGCTGC ACACGTGTGG ACCCCTGCGG CAGGGTCGTG CTCCGTCTCC TGCGGGCGAG
     CCCGTCGTAG TCCTGCCCCC GAGTTCGACG TGTGCACACC TGGGGACGCC GTCCCAGCAC GAGGCAGAGG ACGCCCGCTC

     +1 G  L  M  E  L  R  F  L  C  M  D  S  A  L  R  V  P  V  Q  E  E  L  C  G  L  A  S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
     CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCCACGGA CAGGTCCTTC TCGACACACC GGACCGTTCG
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FIG. 3F

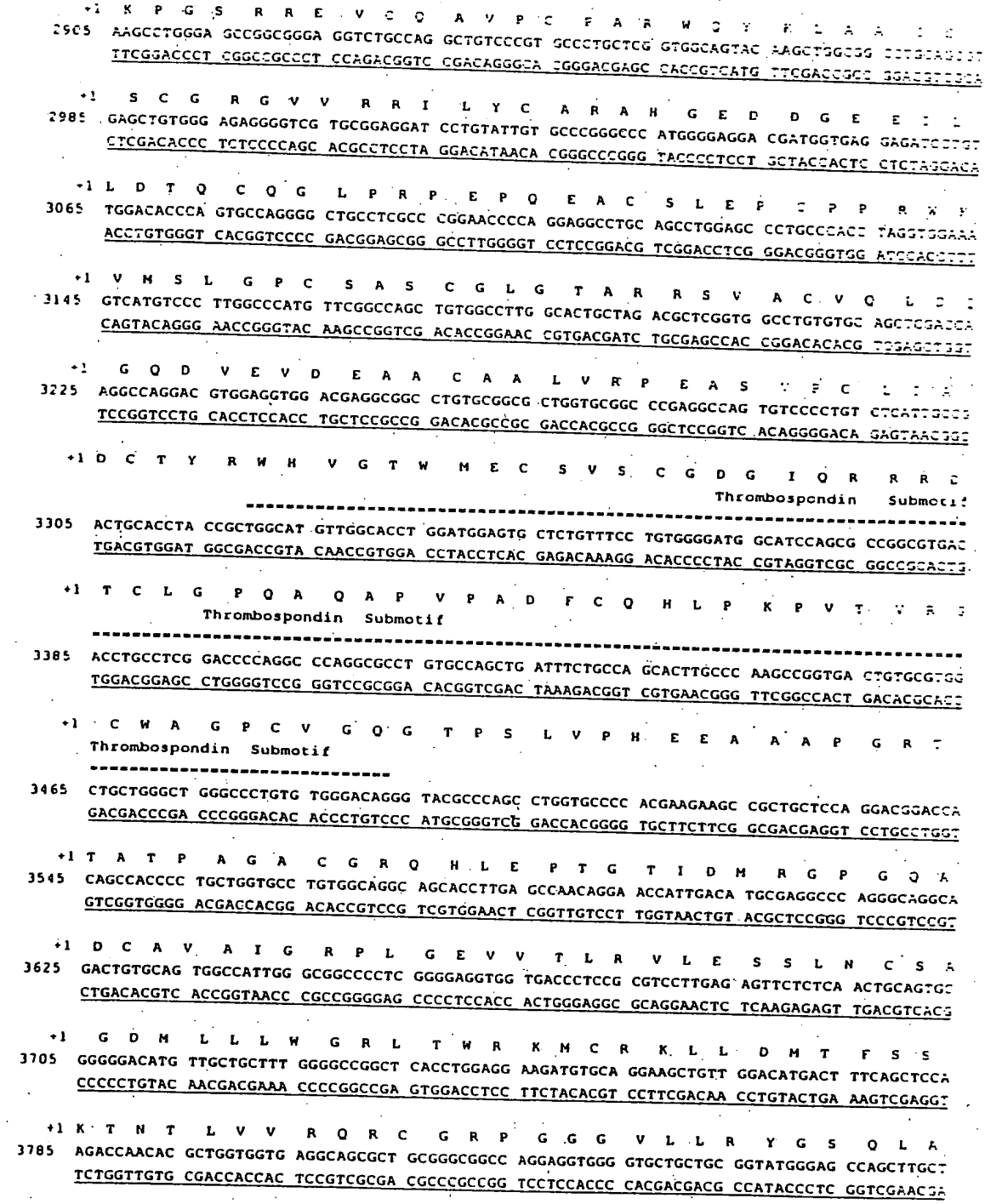

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FIG. 3G

```
   +1  P  E  T  F  Y  R  E  C  D  M  Q  L  F  G  P  W  G  E  I  V  S  P  S  L  S  F  A
3865   CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCCTGGGG TGAAATCGTG AGCCCCTCGC TGAGTCCAGC
       GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTCG

   +1  T  S  N  A  G  G  C  R  L  F  I  N  V  A  P  H  A  R  I  A  I  H  A  L  A  T
3945   CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
       GTGCTCATTA CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

   +1  N  M  G  A  G  T  E  G  A  N  A  S  Y  I  L  I  R  D  T  H  S  L  R  T  T  A  F
4025   ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
       TGTACCCGCG ACCCTGGCTC CCTCGGTTAC GGTCGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTCGCAAG

   +1  H  G  Q  Q  V  L  Y  W  E  S  E  S  S  Q  A  E  M  E  F  S  E  G  F  L  K  A  I
4105   CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
       GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

   +1  A  S  L  R  G  Q  Y  W  T  L  Q  S  W  V  P  E  M  Q  D  P  Q  S  W  K  G  K
4185   GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
       CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GGTTAGTACC CATGGCCTCT ACGTCCTGGG AGTCAGGACC TTCCCTTTCC

   +1  E  G  T
4265   AAGGAACC
       TTCCTTGG
```

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FIG. 4A

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family

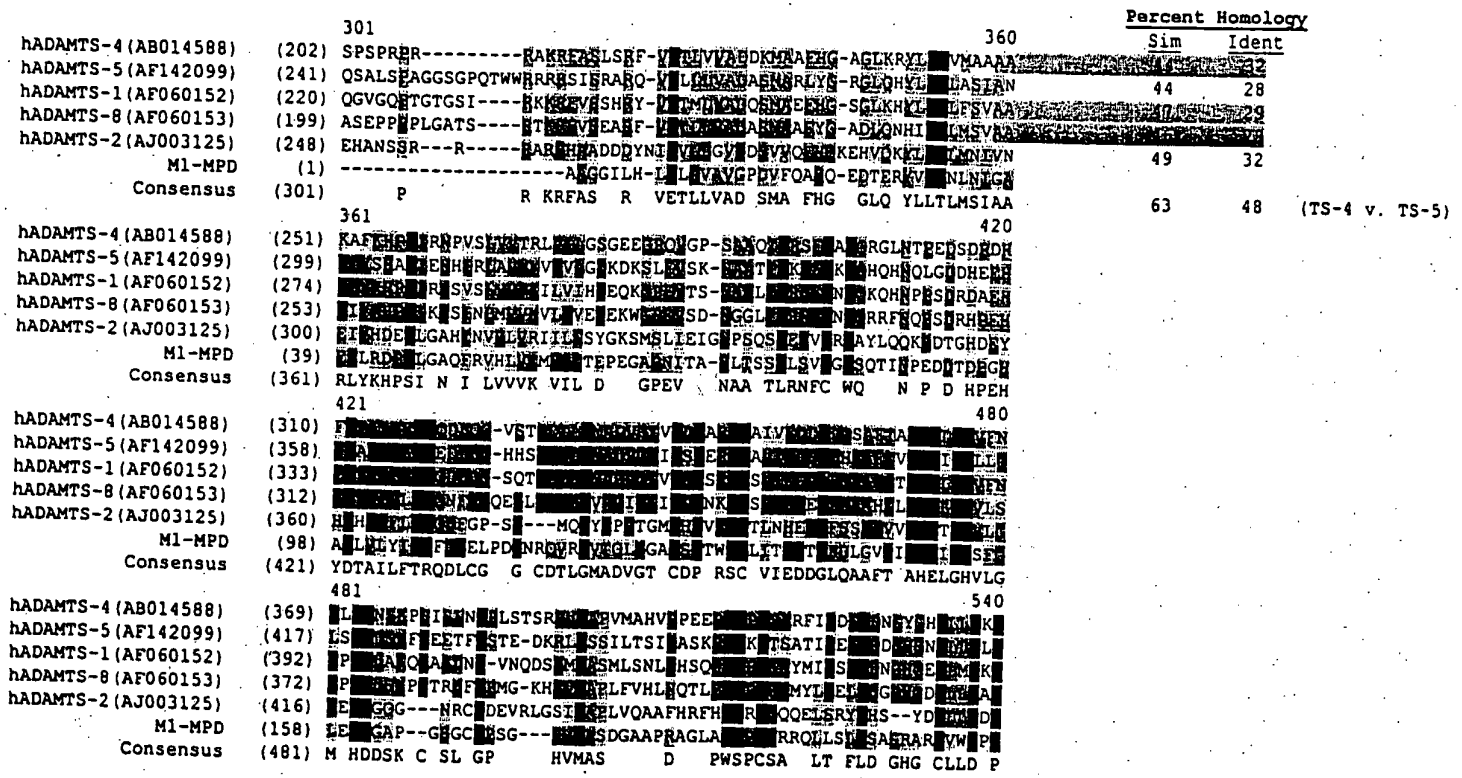
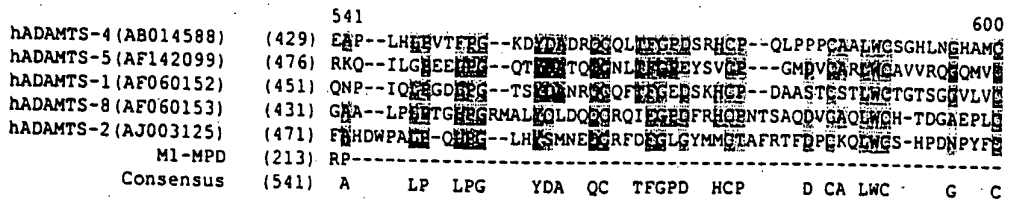


FIG. 4B


541
600
hADAMTS-4(AB014588) (429)
hADAMTS-5(AF142099) (476)
hADAMTS-1(AF060152) (451)
hADAMTS-8(AF060153) (431)
hADAMTS-2(AJ003125) (471)
M1-MPD (213)
Consensus (541) A LP LPG YDA QC TFGPD HCP D CA LWC G C

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~~FIG.1~~ FIG. 1A

CCGGGTCGACCCACGCGTCCGAAGGCCCCCTCTCACTCCGCTCCACTCCTCGGGCTGG
CTCTCCTGAGGATGCACCAGCGTCACCCCCGGGCAAGATGCCCTCCCCTCTGTGTGGC
CGGAATCCTTGCCTGTGGCTTTCTCCTGGGCTGCTGGGGACCCTCCCATTTCCAGCAGA
GTTGTCTTCAGGCTTTGGAGCCACAGGCCGTGTCTTCTTACTTGAGCCCTGGTGCTCCC
TTAAAAGGCCGCCCTCCTTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCGGG
CTGCAGGCGGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCCGATGTCTTCCA
GGCTCACCAGGAGGACACAGAGCGCTATGTGCTCACCAACCTCAACATCGGGGCAGAA
CTGCTTCGGGACCCGTCCCTGGGGGCTCAGTTTCGGGTGCACCTGGTGAAGATGGTCA
TTCTGACAGAGCCTGAGGGTGCTCCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
AGCGTCTGTGGGTGGAGCCAGACCATCAACCCTGAGGACGACACGGATCCTGGCCATG
CTGACCTGGTCCTCTATATCACTAGGTTTGACCTGGAGTTGCCTGATGGTAACCGGCAG
GTGCGGGGCGTCACCCAGCTGGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATTA
CCGAGGACACTGGCTTCGACCTGGGAGTCACCATTGCCCATGAGATTGGGCACAGCTT
CGGCCTGGAGCACGACGGCGCGCCCGGCAGCGGCTGCGGCCCCAGCGGACACGTGA
TGGCTTCGGACGGCGCCGCGCCCCGCGCCGGCCTCGCCTGGTCCCCCTGCAGCCGCC
GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGGCGCGCTGCGTGTGGGACCCGCCGC
GGCCTCAACCCGGGTCCGCGGGGCACCCGCCGGATGCGCAGCCTGGCCTCTACTACA
GCGCCAACGAGCAGTGCCGCGTGGCCTTCGGCCCCAAGGCTGTCGCCTGCACCTTCGC
CAGGGAGCACCTGGATATGTGCCAGGCCCTCTCCTGCCACACAGACCCGCTGGACCAA
AGCAGCTGCAGCCGCCTCCTCGTTCCTCTCCTGGATGGGACAGAATGTGGCGTGGAGA
AGTGGTGCTCCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCCATAGCAGCAGT
GCATGGGCGCTGGTCTAGCTGGGGTCCCCGAAGTCCTTGCTCCCGCTCCTGCGGAGGA
GGTGTGGTCACCAGGAGGCGGCAGTGCAACAACCCCAGACCTGCCTTTGGGGGGCGT
GCATGTGTTGGTGCTGACCTCCAGGCCGAGATGTGCAACACTCAGGCCTGCGAGAAGA
CCCAGCTGGAGTTCATGTCGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC
CTCCCCTGGCGGCGCCTCCTTCTACCACTGGGGTGCTGCTGTACCACACAGCCAAGGG
GATGCTCTGTGCAGACACATGTGCCGGGCCATTGGCGAGAGCTTCATCATGAAGCGTG
GAGACAGCTTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCCGGGAGGACGGGA
CCCTGAGCCTGTGTGTGTCGGGCAGCTGCAGGACATTTGGCTGTGATGGTAGGATGGA
CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGTGGTGGGGACAACAGCACGTGCAGC
CCACGGAAGGGCTCTTTCACAGCTGGCAGAGCGAGAGAATATGTCACGTTTCTGACAGT
TACCCCCAACCTGACCAGTGTCTACATTGCCAACCACAGGCCTCTCTTCACACACTTGG
CGGTGAGGATCGGAGGGCGCTATGTCGTGGCTGGGAAGATGAGCATCTCCCCTAACAC
CACCTACCCCTCCCTCCTGGAGGATGGTCGTGTCGAGTACAGAGTGGCCCTCACCGAG

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FIG. 1B

GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAAACTACAGCTGCCTG
GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTGCGTGCTCGAACCCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCCTGCGGGAGCGGCCAGTGCGC
TGCGTGGAGGCCCAGGGCAGCCTCCTGAAGACATTGCCCCCAGCCCGGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC
AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGACTGAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCTGAGCCCTGTGTCGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG
TCGTGCTCCGTCTCCTGCGGGCGAGGTCTGATGGAGCTGCGTTTCCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTCGTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGGCT
GCCTCGCCCGGAACCCCAGGAGGCCTGCAGCCTGGAGCCCTGCCCACCTAGGTGGAA
AGTCATGTCCCTTGGCCCATGTTCGGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCCTGTGGGGATGGCATCCAGCG
CCGGCGTGACACCTGCCTCGGACCCCAGGCCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGACTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGCCCCTCGGGGAGGT
GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAGGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA
ATGCAGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGGCAGCAGGTGCTCTACTG

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FIG. IC

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

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FIG. 2

PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLLGCWGPSHFQQSCL
QALEPQAVSSYLSPGAPLKGRPPSPGFQRQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINP
EDDTDPGHADLVLYITRFDLELPDGNRQVRGVTQLGGACSPTWSCLITEDTGFDLGVTIAHEI
GHSFGLEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRQLLSLLSAGRARCVWDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLLVPLLDGTECGVEKWCSKGRCRSLVELTPIAAVHGRWSSWGPRSPCSRSCGGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTRCMPSGPREDGTLSLCVS
GSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRAREYVTFLTVTPNLTSV
YIANHRPLFTHLAVRIGGRYVVAGKMSISPNTTYPSLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEEYGNLTRPDITFTYFQPKPRQAWVWAAVRGPCSVSCGAGLRWVN
YSCLDQARKELVETVQCQGSQQPPAWPEACVLEPCPPYWAVGDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQPAVALETCNPQPCPARWEVSEPSSCTSAGGAGLAL
ENETCVPGADGLEAPVTEGPGSVDEKLPAPEPCVGMSCPPGWGHLDATSAGEKAPSPWG
SIRTGAQAAHVWTPAAGSCSVSCGRGLMELRFLCMDSALRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVVRRILYCARAHGEDDGEEILLDTQCQGLPRPEPQE
ACSLEPCPPRWKVMSLGPCSASCGLGTARRSVACVQLDQGQDVEVDEAACAALVRPEASV
PCLIADCTYRWHVGTWMECSVSCGDGIQRRRDTCLGPQAQAPVPADFCQHLPKPVTVRGC
WAGPCVGQGTPSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCAVAIGR
PLGEVVTLRVLESSLNCSAGDMLLLWGRLTWRKMCRKLLDMTFSSKTNTLVVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAIHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

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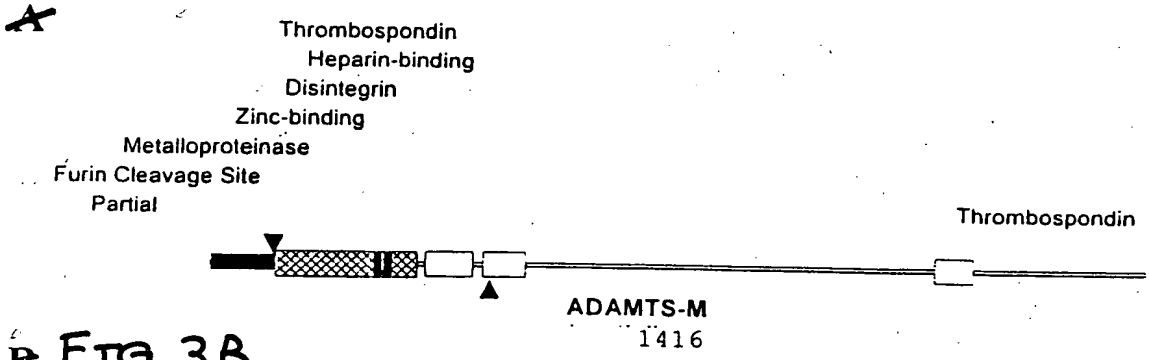
FIG. 3A

Figure 3 FIG. 3A

Domain structure of ADAMTS-M and translated nucleic acid sequence. A) Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). B) FIGS. 3B-3G ADAMTS-M nucleotide sequence with translated amino acid sequence above.

A



B FIG. 3B

```
+1  P  G  R  P  T  R  P  K  A  P  S  H  S  A  P  L  L  G  L  A  L  L  R  M  H  Q  R
                                                                  Partial  Prodomain
    ==========================================================================================
25  CCGGGTCGAC CCACGCGTCC GAAGGCCCCC TCTCACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGCACCAGCG
    GGCCCAGCTG GGTGCGCAGG CTTCCGGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCGC

+1  H  P  R  A  R  C  P  P  L  C  V  A  G  I  L  A  C  G  F  L  L  G  C  W  G  F
                                                      Partial  Prodomain
    ==========================================================================================
105 TCACCCCCGG GCAAGATGCC CTCCCCTCTG TGTGGCCGGA ATCCTTGCCT GTGGCTTTCT CCTGGGCTGC TGGGGACCCT
    AGTGGGGGCC CGTTCTACGG GAGGGGAGAC ACACCGGCCT TAGGAACGGA CACCGAAAGA GGACCCGACG ACCCCTGGGA

+1  S  H  F  Q  Q  S  C  L  Q  A  L  E  P  Q  A  V  S  S  Y  L  S  P  G  A  P  L  K
    Partial Prodomain
    ==========================================================================================
185 CCCATTTCCA GCAGAGTTGT CTTCAGGCTT TGGAGCCACA GGCCGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTTAAAA
    GGGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAACT CGGGACCACG AGGGAATTTT

+1  G  R  P  P  S  P  G  F  Q  R  Q  R  Q  R  Q  R  R  A  A  G  G  I  L  H  L  E  L
                                  Furin Cleavage Site  (Motif)
                                  ==============
    Partial Prodomain                                          Metalloproteinase  Domain
    ==========================================================================================
265 GGCCGCCCTC CTTCCCCTGG CTTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
    CCGGCGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA

+1  L  V  A  V  G  P  D  V  F  Q  A  H  Q  E  D  T  E  R  Y  V  L  T  N  L  N  I
                                                      Metalloproteinase  Domain
    ==========================================================================================
345 GCTGGTGGCC GTGGGCCCCG ATGTCTTCCA GGCTCACCAG GAGGACACAG AGCGCTATGT GCTCACCAAC CTCAACATCG
    CGACCACCGG CACCCGGGGC TACAGAAGGT CCGAGTGGTC CTCCTGTGTC TCGCGATACA CGAGTGGTTG GAGTTGTAGC
```

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FIG. 3C

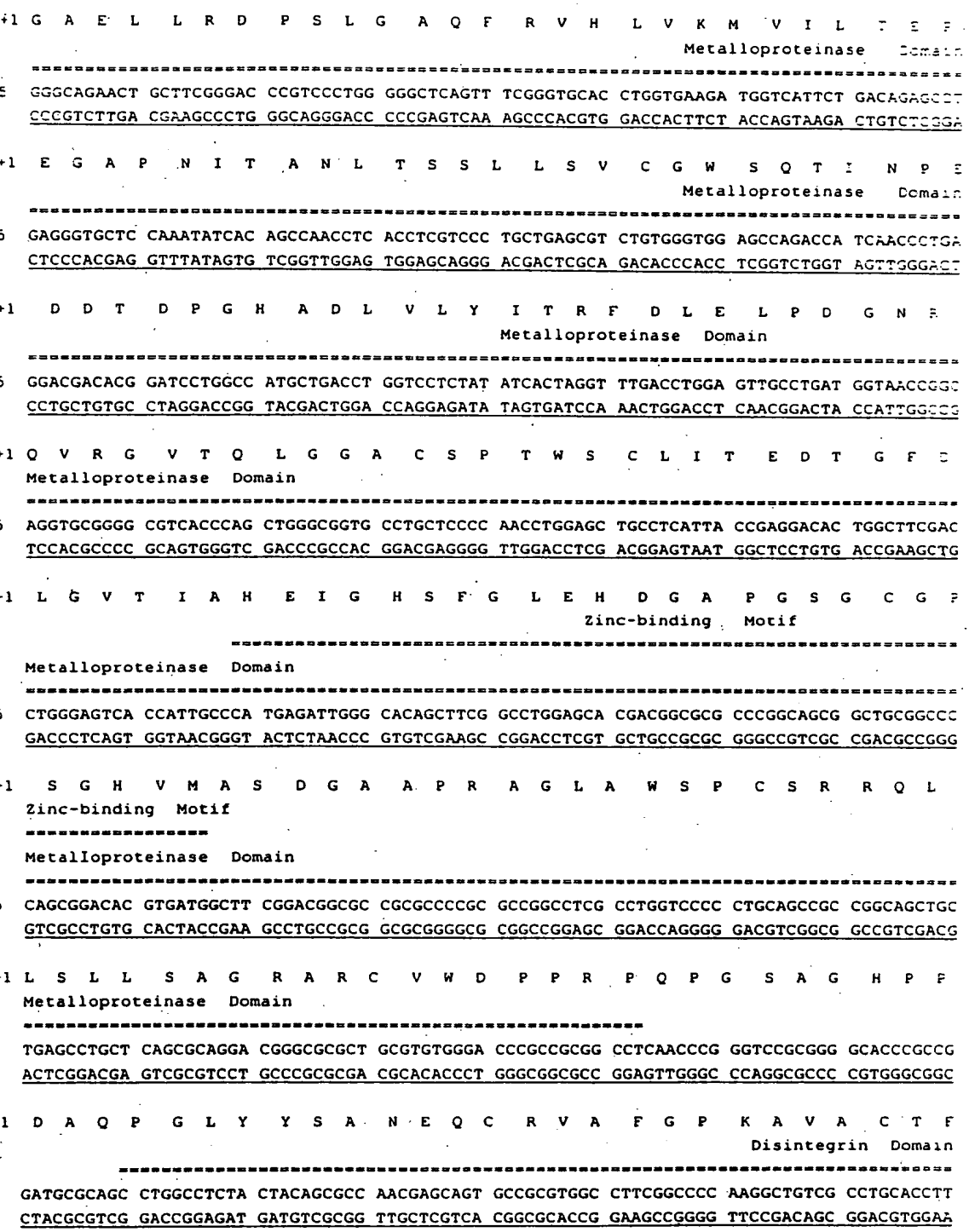

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FIG. 3D

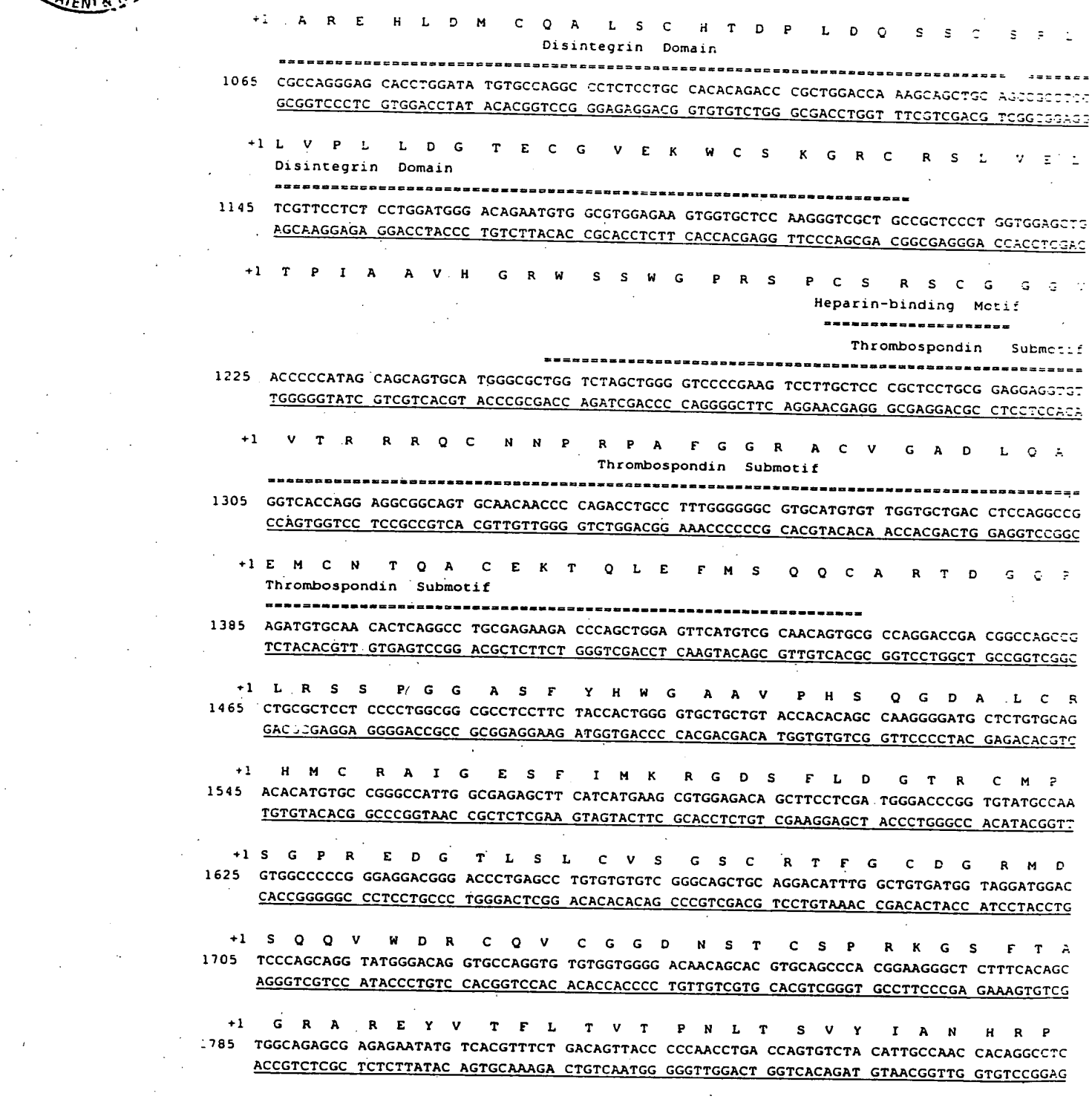

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FIG. 3E

```
    +1 L  F  T  H  L  A  V  R  I  G  G  R  Y  V  V  A  G  K  M  S  I  S  P  N  T  T  T
1965 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCCTAA CACCAGCTAC
     AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGATG

    +1 P  S  L  L  E  D  G  R  V  E  Y  R  V  A  L  T  E  D  R  L  P  R  L  E  E  I  P
1945 CCCTCCCTCC TGGAGGATGG TCGTGTCGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCGCCTGG AGGAGATCCC
     GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTCTAGGT

    +1  I  W  G  P  L  Q  E  D  A  D  I  Q  V  Y  R  R  Y  G  E  E  Y  G  N  L  T  P
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCCGCC
     GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGCTCCT CATACCGTTG GAGTGGGCGG

    +1 P  D  I  T  F  T  Y  F  Q  P  K  P  R  Q  A  W  V  W  A  A  V  R  G  P  C  S  V
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCCTGGGTG TGGGCCGCTG TGCGTGGGCC CTGGTCGGTG
     GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCCGGCGAC ACGCACCCGG GACGAGCCAC

    +1 S  C  G  A  G  L  R  W  V  N  Y  S  C  L  D  Q  A  R  K  E  L  V  E  T  V  Q  I
2185 AGCTGTGGGG CAGGGCTGCG CTGGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
     TCGACACCCC GTCCCGACGC GACCCATTTG ATGTCGACGG ACCTGGTCCG GTCCTTCCTC AACCACCTCT GACAGGTCAC

    +1  Q  G  S  Q  Q  P  P  A  W  P  E  A  C  V  L  E  P  C  P  P  Y  W  A  V  G  P
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGGCG GTGGGAGACT
     GGTTCCCTCG GTCGTCGGTG GTCGCACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCTCTGA

    +1 F  G  P  C  S  A  S  C  G  G  G  L  R  E  R  P  V  R  C  V  E  A  Q  G  S  L  L
2345 TCGGCCCATG CAGCGCCTCC TGTGGGGGTG GCCTGCGGGA GCGGCCAGTG CGCTGCGTGG AGGCCCAGGG CAGCCTCCTG
     AGCCGGGTAC GTCGCGGAGG ACACCCCCAC CGGACGCCCT CGCCGGTCAC GCGACGCACC TCCGGGTCCC GTCGGAGGAC

    +1 K  T  L  P  P  A  R  C  R  A  G  A  Q  Q  P  A  V  A  L  E  T  C  N  P  Q  P  C
2425 AAGACATTGC CCCCAGCCCG GTGCAGAGCA GGGGCCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCCAGCCCTG
     TTCTGTAACG GGGGTCGGGC CACGTCTCGT CCCCGGGTCG TCGGTCGACA CCGCGACCTT TGGACGTTGG GGGTCGGGAC

    +1  P  A  R  W  E  V  S  E  P  S  S  C  T  S  A  G  G  A  G  L  A  L  E  N  E  T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCCAG CTCATGCACA TCAGCTGGTG GAGCAGGCCT GGCCTTGGAG AACGAGACCT
     GGGACGGTCC ACCCTCCACA GTCTCGGGTC GAGTACGTGT AGTCGACCAC CTCGTCCGGA CCGGAACCTC TTGCTCTGGA

    +1 C  V  P  G  A  D  G  L  E  A  P  V  T  E  G  P  G  S  V  D  E  K  L  P  A  P  E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGACTGA GGGGCCTGGC TCCGTAGATG AGAAGCTGCC TGCCCCTGAG
     CACACGGTCC CCGTCTACCG GACCTCCGAG GTCACTGACT CCCCGGACCG AGGCATCTAC TCTTCGACGG ACGGGGACTC

    +1  P  C  V  G  M  S  C  P  P  G  W  G  H  L  D  A  T  S  A  G  E  K  A  P  S  P  W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CCTCCCCATG
     GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCCGGTAG ACCTACGGTG GAGACGTCCC CTCTTCCGAG GGAGGGGTAC

    +1  G  S  I  R  T  G  A  Q  A  A  H  V  W  T  P  A  A  G  S  C  S  V  S  C  G  R
2745 GGGCAGCATC AGGACGGGGG CTCAAGCTGC ACACGTGTGG ACCCCTGCGG CAGGGTCGTG CTCCGTCTCC TGCGGGCGAG
     CCCGTCGTAG TCCTGCCCCC GAGTTCGACG TGTGCACACC TGGGGACGCC GTCCCAGCAC GAGGCAGAGG ACGCCCGCTC

    +1 G  L  M  E  L  R  F  L  C  M  D  S  A  L  R  V  P  V  Q  E  E  L  C  G  L  A  S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
     CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCCACGGA CAGGTCCTTC TCGACACACC GGACCGTTCG
```

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FIG. 3F

```
+1  K  P  G  S  R  R  E  V  C  Q  A  V  P  C  P  A  R  W  Q  Y  R  L  A  A  C  C
2905 AAGCCTGGGA GCCGGCGGGA GGTCTGCCAG GCTGTCCCGT GCCCTGCTCG GTGGCAGTAC AAGCTGGCGG CCTGCAGCCT
     TTCGGACCCT CGGCCGCCCT CCAGACGGTC CGACAGGGCA CGGGACGAGC CACCGTCATG TTCGACCGCC GGACGTCGGA

+1  S  C  G  R  G  V  V  R  R  I  L  Y  C  A  R  A  H  G  E  D  D  G  E  E  I  L
2985 GAGCTGTGGG AGAGGGGTCG TGCGGAGGAT CCTGTATTGT GCCCGGGCCC ATGGGGAGGA CGATGGTGAG GAGATCCTGT
     CTCGACACCC TCTCCCCAGC ACGCCTCCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA

+1  L  D  T  Q  C  Q  G  L  P  R  P  E  P  Q  E  A  C  S  L  E  P  C  P  P  R  W  P
3065 TGGACACCCA GTGCCAGGGG CTGCCTCGCC CGGAACCCCA GGAGGCCTGC AGCCTGGAGC CCTGCCCACC TAGGTGGAAA
     ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGGT CCTCCGGACG TCGGACCTCG GGACGGGTGG ATCCACCTTT

+1  V  M  S  L  G  P  C  S  A  S  C  G  L  G  T  A  R  R  S  V  A  C  V  Q  L  D  C
3145 GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTCGGTG GCCTGTGTGC AGCTCGACCA
     CAGTACAGGG AACCGGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TGCGAGCCAC CGGACACACG TCGAGCTGGT

+1  G  Q  D  V  E  V  D  E  A  A  C  A  A  L  V  R  P  E  A  S  V  P  C  L  I  A
3225 AGGCCAGGAC GTGGAGGTGG ACGAGGCGGC CTGTGCGGCG CTGGTGCGGC CCGAGGCCAG TGTCCCCTGT CTCATTGCCG
     TCCGGTCCTG CACCTCCACC TGCTCCGCCG GACACGCCGC GACCACGCCG GGCTCCGGTC ACAGGGGACA GAGTAACGGC

+1  D  C  T  Y  R  W  H  V  G  T  W  M  E  C  S  V  S  C  G  D  G  I  Q  R  R  R
                                                    Thrombospondin  Submotif
    ================================================================================
3305 ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTTCC TGTGGGGATG GCATCCAGCG CCGGCGTGAC
     TGACGTGGAT GGCGACCGTA CAACCGTGGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTCGC GGCCGCACTG

+1  T  C  L  G  P  Q  A  Q  A  P  V  P  A  D  F  C  Q  H  L  P  K  P  V  T  V  R
              Thrombospondin  Submotif
    ================================================================================
3385 ACCTGCCTCG GACCCCAGGC CCAGGCGCCT GTGCCAGCTG ATTTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
     TGGACGGAGC CTGGGGTCCG GGTCCGCGGA CACGGTCGAC TAAAGACGGT CGTGAACGGG TTCGGCCACT GACACGCACC

+1  C  W  A  G  P  C  V  G  Q  G  T  P  S  L  V  P  H  E  E  A  A  A  P  G  R  T
    Thrombospondin  Submotif
    ============================
3465 CTGCTGGGCT GGGCCCTGTG TGGGACAGGG TACGCCCAGC CTGGTGCCCC ACGAAGAAGC CGCTGCTCCA GGACGGACCA
     GACGACCCGA CCCGGGACAC ACCCTGTCCC ATGCGGGTCG GACCACGGGG TGCTTCTTCG GCGACGAGGT CCTGCCTGGT

+1  T  A  T  P  A  G  A  C  G  R  Q  H  L  E  P  T  G  T  I  D  M  R  G  P  G  Q  A
3545 CAGCCACCCC TGCTGGTGCC TGTGGCAGGC AGCACCTTGA GCCAACAGGA ACCATTGACA TGCGAGGCCC AGGGCAGGCA
     GTCGGTGGGG ACGACCACGG ACACCGTCCG TCGTGGAACT CGGTTGTCCT TGGTAACTGT ACGCTCCGGG TCCCGTCCGT

+1  D  C  A  V  A  I  G  R  P  L  G  E  V  V  T  L  R  V  L  E  S  S  L  N  C  S  A
3625 GACTGTGCAG TGGCCATTGG GCGGCCCCTC GGGGAGGTGG TGACCCTCCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
     CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACTC TCAAGAGAGT TGACGTCACG

+1  G  D  M  L  L  L  W  G  R  L  T  W  R  K  M  C  R  K  L  L  D  M  T  F  S  S
3705 GGGGGACATG TTGCTGCTTT GGGGCCGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
     CCCCCTGTAC AACGACGAAA CCCCGGCCGA GTGGACCTCC TTCTACACGT CCTTCGACAA CCTGTACTGA AAGTCGAGGT

+1  K  T  N  T  L  V  V  R  Q  R  C  G  R  P  G  G  G  V  L  L  R  Y  G  S  Q  L  A
3785 AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
     TCTGGTTGTG CGACCACCAC TCCGTCGCGA CGCCCGCCGG TCCTCCACCC CACGACGACG CCATACCCTC GGTCGAACGA
```

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FIG. 3G

```
   +1  P  E  T  F  Y  R  E  C  D  M  Q  L  F  G  P  W  G  E  I  V  S  P  S  L  S  F  A
3865   CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCCTGGGG TGAAATCGTG AGCCCCTCGC TGAGTCCAGC
       GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTCG

   +1  T  S  N  A  G  G  C  R  L  F  I  N  V  A  P  H  A  R  I  A  I  H  A  L  A  T
3945   CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
       GTGCTCATTA CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

   +1  N  M  G  A  G  T  E  G  A  N  A  S  Y  I  L  I  R  D  T  H  S  L  R  T  T  A  F
4025   ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
       TGTACCCGCG ACCCTGGCTC CCTCGGTTAC GGTCGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTCGCAAG

   +1  H  G  Q  Q  V  L  Y  W  E  S  E  S  S  Q  A  E  M  E  F  S  E  G  F  L  K  A  L
4105   CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
       GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

   +1  A  S  L  R  G  Q  Y  W  T  L  Q  S  W  V  P  E  M  Q  D  P  Q  S  W  K  G  K
4185   GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
       CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GGTTAGTACC CATGGCCTCT ACGTCCTGGG AGTCAGGACC TTCCCTTTCC

   +1  E  G  T
4265   AAGGAACC
       TTCCTTGG
```

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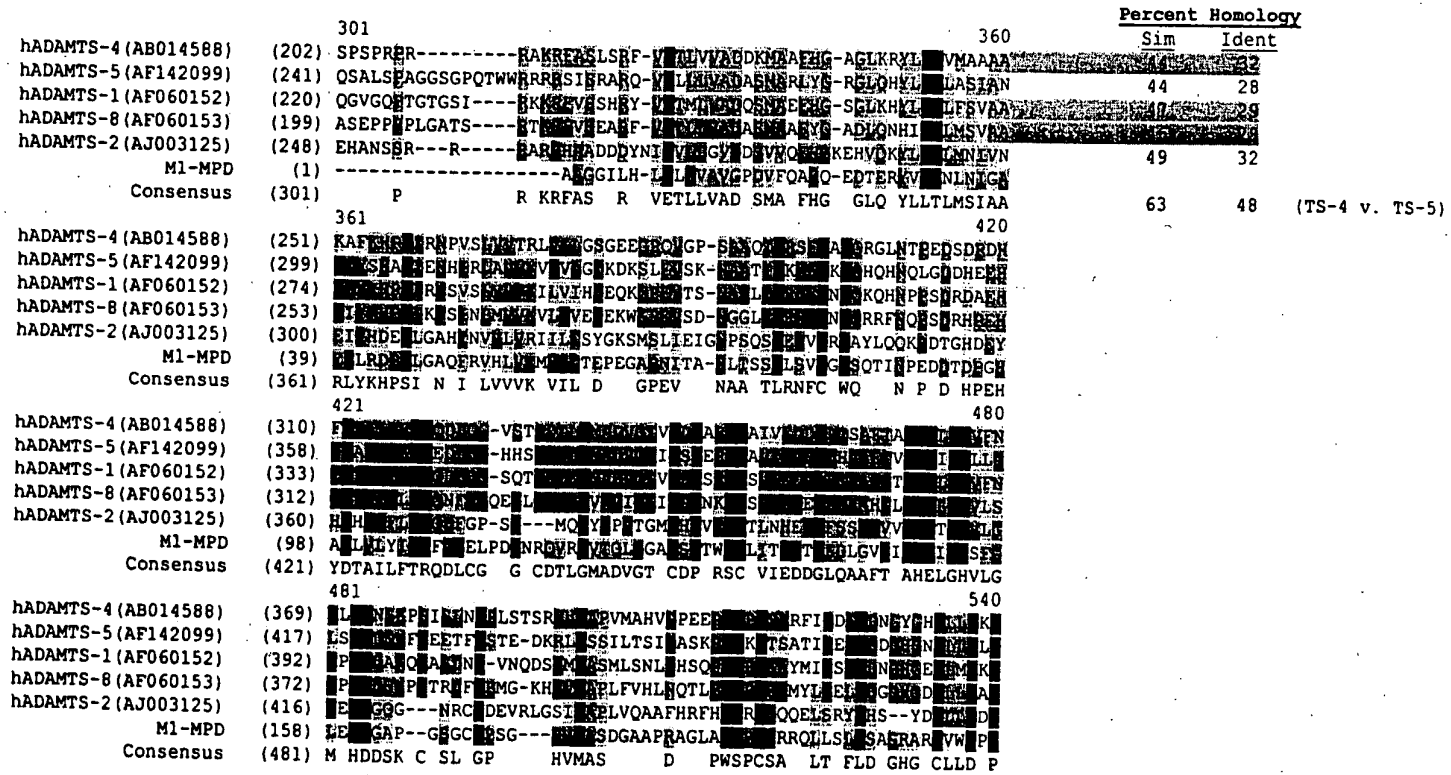
Fig. 4 FIG. 4A

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family



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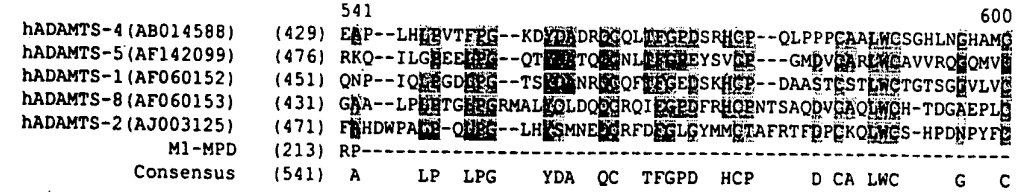
FIG. 48